REMARKS/ARGUMENTS

In response to the Office Action of June 16, 2006, Applicants request re-examination and reconsideration of this application for patent pursuant to 35 U.S.C. 132.

Claim Status/Support for Amendments

The Examiner has indicated that claim 1 is allowable. Claim 36 has been amended. Claims 2-35 were cancelled in a previous Response filed on June 13, 2003. Claims 1 and 36-43 are under examination and remain pending in the instant application.

No new matter has been added by the amendments to claim 36 made herein.

Claim 36 has been amended to clarify that the claimed method involves comparing the characteristic mass spectral profile of the biopolymer marker consisting of amino acid residues 2-12 of SEQ ID NO:1 (shown in Figure 2) to profiles obtained from a mass spectrometric analysis of an unknown sample in order to determine if the claimed biopolymer marker is present in the sample and thus indicative of myocardial infarction (MI), intracerebral hemorrhage (ICH) or congestive heart failure (CHF).

Previous Rejections

The Examiner has withdrawn the rejection of claim 1 as being directed to non-statutory matter. The Examiner has also withdrawn the rejection of claims 1 and 36 as vague and indefinite.

Additionally, there was a third rejection presented in the previous Office Action mailed on January 3, 2006, a rejection of claims 41-43 as failing to comply with the written description requirement (new matter), that the Examiner does not mention in the current Office Action (mailed June 16, 2006).

Applicants respectfully request the Examiner to clarify that rejection of claims 41-43, as failing to comply with the written description requirement, is also withdrawn.

Rejection under 35 USC 112, first paragraph

Claims 36-43, as presented on March 30, 2006, stand rejected under 35 USC 112, first paragraph as failing to comply with the enablement requirement. The claims allegedly contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, the make and/or use the invention.

In *In re Wands* (8 USPQ 2d 1400; CAFC 1988) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in determination of "undue

experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the instant claims the Examiner alleges:

(a) In order to use the claimed invention one of skill in the art must identify a specific amino acid sequence from a mass spectrometry peak that relates only the mass to charge ratio. For the reasons discussed below, there would be an unpredictable amount of experimentation required to practice the claimed invention.

(b) The description does not provide detailed guidance as to how to confirm a specific amino acid sequence with a mass spectrometry peak that only provides mass to charge ratio information.

(c) The description does not provide working examples of confirming a specific amino acid sequence from a mass spectrometry peak.

(d) The nature of the invention, of confirming a specific polypeptide sequence required knowledge of the specific ordering of amino acids in the sequence.

(e) The prior art shows that mass spectrometry can give

information of the mass to charge ratio of polypeptide fragments, however, determining the exact sequences from a single mass spectrometry peak is not taught.

(f) The skill of those in the art of polypeptide sequence characterization is high.

(g) The predictability of the relationship of connection of the location of a single mass spectrometry peak (i.e. the polypeptide mass) to the exact sequence that confirms a specific polypeptide is unknown in the prior art.

(h) The claims are broad in that they do not specify how an exact polypeptide sequence can be confirmed from only a single mass spectrometry peak.

The skilled practitioner would first turn to the instant description for guidance in using the claimed invention. However, the description lacks clear evidence that a specific sequence of amino acids in a particular order can be determined from a single mass spectrometry peak. As such, the skilled practitioner would turn to the prior art for such guidance, however, the prior art does not discuss the determination of amino acid arrangements from one mass spectrometry peak. Finally, said practitioner would to trial and error experimentation to confirm the polypeptide sequence claimed. Such amounts to undue experimentation.

The Examiner further asserts that claim 36 step c recites

"confirming the presence of..amino acid residues 2-12 of SEQ ID NO:1 in said sample by identifying a mass spectral profile having an ion peak at about 1348 daltons..." The mass spectrometry peak at 1348 (or about 1348) is used to confirm the presence of the specific polypeptide with the sequence disclosed and described on page 31, lines 13-16 of the specification. However, the use of the mass spectrometry peak at "about 1348" for the confirming of said sequence is not enabled because a sequence with the same amino acids but in a different order of arrangement would also be detected at 1348 daltons. Additionally, a similar amino acid sequence with slight modification could also potentially have a mass "of about 1348" daltons. Therefore, the identification of the peak does not confirm the presence of the claimed sequence in the sample.

Applicants respectfully disagree with the Examiner's assertions.

The claimed biopolymer marker, a peptide fragment having a molecular weight of about 1348 daltons, was resolved from serum samples using Surface-Enhanced Laser Desorption Ionization (SELDI) mass spectrometric techniques (see the instant specification at pages 20-27 and Figure 2). This peptide fragment was observed to be present in disease states and absent in normal states and thus, was deemed to be in some way evidentiary of these disease states

(see the instant specification at pages 26-27 and Figure 1). The peptide was then purified and sequenced using tandem mass spectrometric techniques. The sequence HRIHWESASLL (amino acid residues 2-12 of SEQ ID NO:1) was identified as a fragment of complement C3 protein (see the instant specification at page 27, line 6 to page 28, line 2). Methods for determining peptide sequence by comparing data obtained from tandem mass spectrometry to a library of known proteins are well-known and commonly practiced (see, for example, US Patent 5,538,897; reference 1). Thus, it is clear that the application discloses the specific amino acid sequence of the peptide (amino acid residues 2-12 of SEQ ID NO:1) corresponding to the mass spectral peak at about 1348 daltons shown in Figure 2.

It is necessary to point out that mass spectral profiles are reproducible; many have been published and/or stored in data bases for use as references, i.e. an unknown mass spectral profile can be searched against those profiles in a database for potential matches (see attached article "A Primer on Mass Spectrometers" by Peggy Knight, accessed from the website of the U.S. Environmental Protection Agency on September 11, 2006; reference 2). A match between an unknown mass spectral profile and a known mass spectral profile (found in a library and/or database) will in turn identify the peptide represented in the profile.

The instant specification provides a mass spectral profile, shown in Figure 2, characteristic of the claimed biopolymer marker (amino acid residues 2-12 of SEQ ID NO:1), which is intended to be used as a reference to determine the presence of the biopolymer marker in an unknown sample. The mass spectral profile of the claimed biopolymer marker exhibits an ion peak at about 1348 daltons and the presence of this biopolymer marker is confirmed by identification of the 1348 dalton peak in a mass spectral profile obtained from a sample. In this way, identification of this mass spectral profile diagnoses myocardial infarction, intracerebral hemorrhage, or congestive heart failure, for example, if the mass spectral profile shown in Figure 2 is found in a mass spectral profile obtained from an unknown sample, then the claimed biopolymer marker (amino acid residues 2-12 of SEQ ID NO:1) is determined to be present in the sample and the patient from which the sample was obtained is diagnosed with myocardial infarction, intracerebral hemorrhage or congestive heart failure.

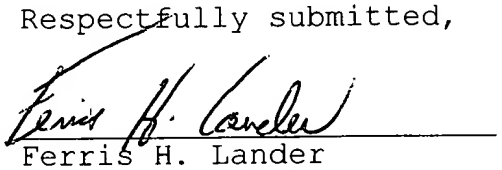
Thus, the instant specification provides a working example of confirming the presence of a specific amino acid sequence (amino acid residues 2-12 of SEQ ID NO:1) from a known mass spectral profile(shown in Figure 2). Applicants assert that an artisan of ordinary skill, when reviewing the instant specification and given the high level of knowledge and skill in the art, would know how

to use the mass spectral profile of the claimed biopolymer marker, as shown in Figure 2, as a reference to identify the marker in unknown samples. Accordingly, Applicants respectfully request that this rejection under 35 USC 112, first paragraph now be withdrawn.

CONCLUSION

In light of the foregoing remarks and amendments to the claims, it is respectfully submitted that the Examiner will now find the claims of the application allowable. Favorable reconsideration of the application is courteously requested.

Respectfully submitted,



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